04:30

726-3 Functional Mitral Regurgitation Correlates with Incomplete Mitral Valve Closure not Left Ventricular Sphericity in Active Myocarditis

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Incomplete mitral valve (MV) closure and LV sphericity correlates with functional MR in chronic dilated cardiomyopathy. To assess the mechanism of MR in active myocarditis (M) echocardiograms performed within 5.7 ± 1.2 days of initial RV biopsy in 27 pts with histologically proven M enrolled in the Myocarditis Treatment Trial were analyzed. M pts were stratified into those with mild MR (≤1+, n = 14) and moderate MR (≥2+, n = 13). LV volume (vol) was measured and a sphericity index (SI) calculated. A value approaching 1 represents increased sphericity. Mitral annular (MA) diameter (d), the distance (DIS) between MV leaflet coaptation and MA plane, and the area enclosed by MV and MA (MVarea) were measured and compared to 20 normal controls.

	MAd (cm)	DIS (cm)	MVarea (cm^2)	LVvol (cc/m^2)	SI
Control	2.3 ± 0.2	0.32 ± 0.13	0.34 ± 0.13	49.5 ± 7.9	0.36 ± 0.05
≤1+ MR	3.1 ± 0.4*	0.60 ± 0.14*	1.2 ± 0.45*	79.7 ± 28.9*	0.47 ± 0.10*
≥2+ MR	3.9 ± 0.5*	0.96 ± 0.18*	2.3 ± 0.64*	78.3 ± 29.1*†	0.48 ± 0.09*†

*p < 0.0001 compared to control, †p = NS compared to ≤1+ MR

Conclusion: In active M, functional MR does not correlate with increasing LV sphericity. Incomplete MV closure and MA dilatation are more important correlates of MR severity.

04:45

726-4 Favorable Long-term Outcome of Severe Acute Myocarditis in Children not Receiving Immunosuppressive Therapy. A Comparative Study with Adult Patients

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With the aim to study spontaneous long-term outcome in children with severe acute myocarditis (AM) not receiving immunosuppressive drugs, and to compare children evolution with that of adults with AM, we have prospectively assessed 50 patients (15 children, 35 adults) with AM and severe left ventricular dysfunction (left ventricular ejection fraction [LVEF] <40%) diagnosed in our hospital in the last 8 years. Immunosupressive therapy was not used in any patient. Children age ranged from 2 months to 12 years (mean: 2 ± 3 years). Initial LVEF was 30 ± 12% in children and 28 ± 10% in adults (NS). After a follow-up of 21 ± 16 months (range: 1–80), 3 children (20%) and 9 adults (26%) died or required heart transplantation (HT). Probability of being alive and free from HT at 2 years was 75% in children and 60% in adults. LVEF rose at 1 month to 45 ± 14% in children and to 36 ± 13% in adults ($p < 0.05$), and to 58 ± 15% in children and 40 ± 16 in adults at the end of follow-up ($p < 0.01$). Unfavorable outcome (death, HT or chronic dilated cardiomyopathy with LVEF <45%) occurred in 4 children (16%) and 16 adult patients (46%) ($p < 0.05$). A lower (<30%) 1-month LVEF and an unfavorable 1-month evolution were the most powerful predictors of non-favorable long-term outcome ($p < 0.001$). In conclusion, long-term evolution of children with severe AM not receiving immunosuppressive drugs is favorable in most cases, and it appears to be better than in adults. Nevertheless, patients in whom LVEF does not improve at short-term appear to be at higher risk for death, and they should be considered for HT.

05:00

726-5 Autoantibodies to Stress Proteins in Dilated Cardiomyopathy and Biopsy Proven Myocarditis

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Stress proteins are synthesized either constitutively or in response to heat shock or other metabolic insults. Stress proteins are immunodominant antigens of mycobacteria and other nonviral microorganisms and have been highly conserved during evolution. Stress proteins have therefore been thought to be involved in the pathogenesis of various autoimmune diseases.

As myocarditis and dilated cardiomyopathy (DCM) are both thought to be initiated by autoimmune mechanisms, we looked for autoantibodies to stress proteins. Through their exposed situation in the vasculature, endothelial cells may participate in the initiation of these diseases. We therefore used both purified stress proteins and stressed endothelial cells as antigenic substrate.

Methods: Sera were obtained from healthy controls and patients with dilated cardiomyopathy and biopsy proven myocarditis. Endothelial cells were isolated from umbilical veins by collagenase digestion, cultivated to the 2nd or 3rd passage, and then subjected to a heat shock (45°C, 15 min). The cells were allowed to recover for 16 h at 37°C, scraped off the culture vessel, and lysed in an urea buffer. The cell lysate or purified hsp 90 and 27 was then used in a 1D and 2D-immunoblot.

Results:

Diagnosis	N	Antibodies against		
		purified hsp 27	hsp 90	cell lysate
DCM	113	15/13%	4/3.5%	41/36%
Myocarditis	62	9/14.5%	4/6.5%	38/61%
Controls	96	9/9%	7/7%	23/24%

Conclusion: In the sera of patients with DCM and myocarditis antibodies to endothelial proteins were found, indicating that antiendothelial antibodies may be involved in the pathogenesis of these diseases. In contrast, autoantibodies to stress proteins were not found in significantly higher number in the sera of patients as compared to healthy controls. A role of autoantibodies to hsp 27 and hsp 90 in the pathogenesis of these diseases can thus not be assumed.

05:15

726-6 Diastolic Left Ventricular Function Improves in Patients with Healed Myocarditis Compared to Patients with Ongoing Myocarditis

Christiana M. Schannwell [1], Igor Janda [1], Uwe Kühl [1], Nicola Roediger [1], Otto N. Krogmann [1], Markus Jacob [2], Heinz-P. Schultheiss [1], Bodo E. Strauer [1]. [1] *University Düsseldorf, Germany;* [2] *University Zürich, Switzerland*

In order to evaluate whether there are hemodynamic differences between patients (P) with healed or ongoing myocarditis (MC) biplane LV-angiocardiography and high fidelity pressure measurements were performed in 49 P compared to 12 controls (C). Diagnosis of MC was based on clinical presentation and right ventricular endomyocardial biopsy (lymphocytic infiltration, enhanced expression of human class 1 and 2 antigens). In the follow-up (FU) biopsy after 3 months lymphocytic infiltration resolved in 16 P (P1), and persisted in 33 P (P2). Systolic and diastolic LV-function in P with MC was depressed when compared to C. At FU LV-ejection fraction did not increase whereas diastolic LV-function (time constant of relaxation (T;ms), constant of myocardial stiffness (b)) did improve significantly in P1 whereas it remained unchanged or even decreased in P2. However it was still depressed when compared to C.

	EF	LMMI	LVEDP	LVEDVI	T	b	
C	64	86	11	86	45	11	
	FU	FU	FU	FU	FU	FU	
P1	48°52°	148*°122°	18*°13	146*°128°	103*°59†°	35*° 18†	
P2	49°50°	146°141°	20°19°	142°141°	90°91°	36*°	51°

EF: LV-ejection fraction (%), LMMI: LV-muscle mass index (g/m^2), LVEDVI: LV-enddiastolic volume index (ml/m^2), LVEDP: LV-enddiastolic pressure (mmHg); *: $p < 0.05$ vs. FU, †: $p < 0.05$ vs P2, °: $p < 0.05$ vs C

Conclusion: The healing process in myocarditis seems to improve active and passive LV diastolic properties before LV systole is positively effected.

727 Endogenous Influence on Failing Intact Myocardium

Monday, March 20, 1995, 4:00 p.m.–5:30 p.m.
Ernest N. Morial Convention Center, Room 61

04:00

727-1 The Role of Sympathetic Activity in Murine Myocarditis Leading to the Development of Dilated Cardiomyopathy

A. Shakir Pandey, Michael J. Sole, John S. Floras, Fayez Dawood, Wen-Hu Wen, Lily Wee, Peter Liu. *The Toronto Hospital, Centre for Cardiovascular Research, University of Toronto, Canada*

Sympathetic activation occurs in heart failure, but it is not known how much this process actually contributes to the *development* of cardiomyopathy. Accordingly we tested the effect of total peripheral ganglionic blockade using a novel approach with oral Chlorisondamine (Chlor) in a murine model of myocarditis-dilated cardiomyopathy. Chlorisondamine inhibits sympathetic output at the peripheral level. DBA/2 mice (n = 110) received 10 pfu of encephalomyocarditis virus and were randomized to Chlor (100 mg/kg p.o. start-